PSJH Human Research Protection Program (HRPP)
Guidance on the Use of Electronic Informed Consent

Introduction

This Guidance draws heavily from the Food and Drug Administration's (FDA) *Use of Electronic Informed Consent Questions and Answers* Guidance for Institutional Review Boards, Investigators, and Sponsors (December 2016). For the purposes of this guidance, electronic informed consent (eIC) refers to the use of electronic systems and processes that may employ multiple electronic media, including SmartPhones, iPads and equivalents, electronic data capturing systems, and interactive Web sites, to convey information related to the study and to obtain and document informed consent. This guidance clarifies that when implementing an eIC, a variety of approaches may be used to fulfill HHS and FDA regulatory requirements for informed consent and IRB review (45 CFR part 46 and 21 CFR parts 50 and 56) and FDA regulations for electronic records and electronic signatures (21 CFR part 11).
This guidance is written with the following objectives:

- Ensure protection of the rights, safety, and welfare of human subjects
- Facilitate the subject's comprehension of the information presented during the eIC process
- Ensure that appropriate documentation of consent is obtained when electronic systems and processes that may employ multiple electronic media are used to obtain informed consent
- Outline the requirements for IRB review of studies utilizing eIC

Background

The term *informed consent* is often mistakenly viewed as synonymous with obtaining a handwritten signature from the subject or the subject's legally authorized representative (LAR) on a written informed consent form. However, obtaining a subject's oral or written informed consent is only part of the overall informed consent process. Informed consent involves providing a potential subject with adequate information about the research to allow for an informed decision about the subject's voluntary participation in a research study. Informed consent must include a process that facilitates the subject's comprehension of the information and allows adequate opportunity for the subject to ask questions and consider whether or not to participate (45 CFR 46.116 and 21 CFR 50.20). Furthermore, this process often continues beyond obtaining the subject's initial consent at the time of enrollment and may involve providing additional information as the research progresses or as the subject or situation requires. The elements of informed consent for human subjects and the requirements for documentation of informed consent are discussed in 45 CFR 46.116 and 46.117 and 21 CFR 50.25 and 50.27, respectively.

The research community is showing increasing interest in using electronic media to supplement or replace paper-based informed consent processes. An eIC may be used to provide information usually contained within the written informed consent document, evaluate the subject's comprehension of the information presented, and document the consent of the subject or the subject's LAR. Electronic processes to obtain informed consent may use an interactive interface, which may facilitate the subject's ability to retain and comprehend the information. Furthermore, these electronic processes may allow for rapid notification to the subjects of any amendments pertaining to the informed consent that may affect their willingness to continue to participate. Electronic processes may also promote timely entry of any eIC data into a study database and allow for timely collection of the subject's informed consent data from remote locations.

Presentation of Information

The eIC must contain all elements of informed consent required by the Department of Health and Human Services (HHS) and/or FDA regulations (45 CFR 46.116 and 21 CFR 50.25). The information must be in language understandable to the potential subject or the subject's LAR and conveyed in a manner that minimizes the possibility of coercion or undue influence regarding the subject's decision to participate in a study (45 CFR 46.116 and 21 CFR 50.20). *Understandable* means that the information presented to subjects is in a language and at a level the subject can comprehend, including an explanation of scientific and medical terms. To ensure that the eIC is presented appropriately and that subjects will have enough time to dedicate to the eIC process, the subjects should be informed of approximately how long the process will take and what information will be presented to them.

Any eIC should be easy to navigate, allowing the user to proceed forward or backward within the system and to stop and continue at a later time. Hyperlinks may be provided where helpful. The eIC may also incorporate electronic strategies to encourage subjects to access all of the consent material before documenting their consent.

Electronic informed consent may be used to either supplement or replace paper-based informed consent processes in order to best address the subject's needs throughout the course of the study. For example, some subjects may prefer one method over another. Other subjects may have difficulty navigating or using electronic systems because of, for example, a lack of familiarity with electronic systems, poor eyesight, or impaired motor skills. In such cases, the eIC process may not be appropriate for these subjects. Therefore, subjects should have the option to use paper-based or electronic informed consent methods completely or partially throughout the informed consent process. Moreover, in some circumstances, it may be appropriate for investigators or study personnel to assist subjects in using the eIC technology. For example, study personnel may help the subject navigate the consent by clicking on links for the subject.

The eIC Process

The investigator is responsible for ensuring that legally effective informed consent is obtained before that subject takes part in the study (see 45 CFR 46.116 and 21 CFR 50.20, 312.60, and 812.100). If

the investigator delegates this responsibility, the responsibility should be delegated to an individual qualified by education, training, and experience to perform this activity. Whether part or all of the eIC process takes place on-site or remotely, the responsibility for obtaining informed consent remains with the investigator and the study personnel to which responsibility has been appropriately delegated. The investigator cannot delegate authority to obtain informed consent to the electronic system.

The consent process may take place at the study site when both the investigator and subject are at the same location, or it may take place remotely (e.g., at the subject's home or another convenient venue) where the subject reviews the consent document in the absence of the investigator. The eIC materials may be provided for both on-site and remote access.

If the entire process takes place at the study site, the study personnel can personally verify the subject's identification, review the eIC content, answer questions about the material, have follow-up discussions, and witness the signing of the eIC.

If any or all of the consent process takes place remotely and is not personally witnessed by study personnel, the electronic system must include a method to ensure that the person electronically signing the informed consent is the subject who will be participating in the research study or is the subject's LAR (see 21 CFR 11.100(b)). Examples of various methods that could be used include verification of a state-issued identification or other identifying documents or use of personal questions, biometric methods, or visual methods.

Facilitating the Subject's Understanding of the Information Being Presented

To assist the subject in understanding the material, the eIC may use interactive electronic-based technology, which may include diagrams, images, graphics, videos, and narration. The eIC should be appropriate for the intended audience, taking into consideration the subject's age, language, and comprehension level.

The eIC may contain various methods to help an investigator assess the subject's understanding of the information being presented during the eIC process. For example, the eIC may include optional questions at any time during the eIC discussion that can be used to help educate the subject about the information presented, as well as assess the subject's understanding of the informed consent materials. Such optional questions and other methods may be used as tools to gauge subject comprehension of key study elements and highlight areas where the subject might need further explanation and discussion before signing the informed consent to enter the study.

Documenting Electronic Informed Consent

The procedure for eIC may include an electronic method to capture the signature of the subject or the subject's LAR. The Office for Human Research Protections (OHRP) and FDA regulations permit the use of electronic signatures when written informed consent is required. OHRP permits electronic

signatures if such signatures are legally valid within the jurisdiction where the research is to be conducted.

For FDA-Regulated Clinical Investigations

FDA regulations found at 21 CFR part 11 set forth the criteria under which FDA considers electronic records, electronic signatures, and handwritten signatures executed to electronic records to be trustworthy, reliable, and generally equivalent to a handwritten signature executed on paper (see 21 CFR 11.1(a)). In order to be considered equivalent to full handwritten signatures, electronic signatures must comply with all applicable requirements under 21 CFR part 11. The electronic system must also capture and record the date that the subject or subject's LAR provides consent (see 21 CFR 50.27(a)).

The regulations found at 21 CFR part 11 permit a wide variety of methods to create electronic signatures, including using computer-readable ID cards, biometrics, digital signatures, and user name and password combinations. FDA does not mandate or specify any particular methods for electronic signatures, including any particular biometric method upon which an electronic signature may be based.

IRBs, investigators, and sponsors should consider such issues as how the electronic signature is created and whether the informed consent or permission document can be produced in hard copy for review by the subject upon request. IRBs, investigators, and sponsors may rely on a statement from the vendor of the electronic system used for obtaining the electronic signature that describes how the signature is created and that the system meets the relevant requirements contained in 21 CFR part 11.

HHS and FDA regulations require that the person signing the informed consent (i.e., the subject or the subject's LAR or the parents or guardians of subjects who are children) be given a copy of the written informed consent form (45 CFR 46.117(a) and 21 CFR 50.27(a)), unless the requirement for documentation of informed consent has been waived under 45 CFR 46.117(c) and 21 CFR 56.109(c)). Although FDA regulations do not require that the subject's copy include a signature, FDA recommends that a copy of the signed informed consent form that includes the date when the eIC was signed be provided to the subject.

The copy provided to the subject can be paper or electronic and may be provided on an electronic storage device or via email. If the copy provided includes one or more hyperlinks to information on the Internet, the hyperlinks should be maintained and information should be accessible until study completion. Note that if the eIC uses hyperlinks or other Web sites or podcasts to convey information specifically related to the research, the information in these hyperlinks should be included in any printed paper copy, if one is provided.

<u>Privacy, Security, and Confidentiality of the eIC information</u>

For FDA-regulated clinical investigations, the electronic system that supports the eIC must be secure with restricted access (see 21 CFR 11.10 and 11.30) and should include methods to ensure confidentiality regarding the subject's identity, study participation, and personal information after informed consent has been obtained. If the entity holding the subject's personal information is a covered entity under the Health Insurance Portability and Accountability Act of 1996 (HIPAA) (Public Law No. 104-191) or acting as a business associate of a HIPAA-covered entity, the requirements in the HIPAA Privacy, Security, and Breach Notification Rules apply (see 45 CFR parts 160 and 164). For example, the subject's information within an electronic system must be encrypted, unless the entity documents why encryption is not reasonable and appropriate in their specific circumstances and implements a reasonable and appropriate equivalent measure.

Electronic HIPAA Authorizations for Research and Experimental Subject's Bill of Rights

HIPAA authorizations may be obtained electronically, provided that the signature of the subject (or the subject's personal representative) is a valid electronic signature under applicable laws and regulations. The Electronic Signatures in Global and National Commerce Act (E-Sign Act) (Public Law 106-229) addresses what constitutes a valid electronic signature and provides that a signature may not be denied legal effect because it is in electronic form.

The HIPAA Privacy Rule requires that when a covered entity seeks an authorization from a subject (or a subject's personal representative), the covered entity must provide the individual with a copy of the signed authorization; this requirement also applies where a HIPAA authorization is obtained electronically.

Similarly, for research conducted in California, signatures on the Experimental Subject's Bill of Rights may be obtained electronically, and the subject should be provide with a copy of the signed document.

IRB's responsibilities in the eIC process

HHS and FDA regulations require that an IRB review and have authority to approve, require modifications in (to secure approval), or disapprove all research activities covered by the applicable regulations (see 45 CFR 46.109(a) and 21 CFR 56.109(a)). A critical part of this responsibility is for the IRB to ensure there is an adequate informed consent process that protects the rights and welfare of subjects participating in HHS-regulated research and FDA-regulated clinical investigations (see 45 CFR 46.109(b) and 21 CFR 56.109(b) and 56.111(a)(4)). Therefore, the IRB must review and approve the eIC and any amendments to the eIC that the subject will receive and view (see 45 CFR 46.109(a) and 21 CFR 56.109(a)). The IRBs must maintain and retain copies of materials that have been reviewed in accordance with 45 CFR 46.115 and 21 CFR 56.115.

The IRBs should also review any optional questions or methods used to gauge subject comprehension of key study elements. The IRB should also review the usability of the eIC materials to ensure that they are easy to navigate. If the program uses hyperlinks to convey study-related information, IRBs should review the contents to which subjects are referred in order to determine if the study-related

information that has been supplied is accurate and appropriate. Because Web sites are often modified over time, IRBs must maintain the version of the Web site information that contains the study-related information that the IRB reviews and approves, either electronically or as a hard copy (see 45 CFR 46.115 and 21 CFR 56.115).

IRB review of studies utilizing eIC

In accordance with the IRB's responsibilities outlined above, the use of eIC in a study must be reviewed and approved by the IRB. Investigators planning to utilize eIC for a study must describe its use in the application submitted to the IRB and receive IRB approval prior to implementation. At a minimum the information provided to the IRB should indicate the method(s) to be used to obtain consent electronically and the provisions in place to maintain the confidentiality of the electronic consent documents per the standards described above. The content of the eIC materials must be provided to the IRB for review in their entirety.

It is the investigator's responsibility to ensure that the method used to document consent electronically is considered legally effective at their location. Investigators are encouraged to consult with Risk and Integrity Services, and Information Services, as appropriate, for guidance on ensuring their eIC method will be legally effective and that the system used to obtain and store signed eIC documents has sufficient safeguards to ensure confidentiality is maintained.

If you have any questions regarding this Guidance, please contact the PSJH HRPP Office at irbsharedservices@providence.org.